IN THE CLAIMS

Please delete all prior lists of claims in the application and insert the following list of claims:

1. (CANCELED).

2. (CURRENTLY AMENDED) A method for detecting a compound produced by a biosynthetic pathway, comprising:

   i) isolating genomic DNA from a source containing uncultivated microorganisms, without an intervening step of ~~isolating or~~ culturing cells from the source, by mixing the source with an extraction buffer and lysing the microorganisms to obtain isolated genomic DNA; and then

   ii) inserting the isolated genomic DNA of step (i) into a replicable vector to obtain clones of the replicable vector comprising the isolated genomic DNA; and then

   iii) introducing the clones of step (ii) into host cells to obtain a library of host cells, wherein the isolated genomic DNA in at least some of the clones is at least 50 kb; and then

   iv) culturing the host cells of step (iii) under conditions wherein an open reading frame sequence of the isolated genomic DNA is expressed by the host cells; and then

   v) detecting a compound produced by the host cells as a result of expression of the open reading frame sequence of step (iv).

3. (PREVIOUSLY PRESENTED) The method of claim 2, wherein step (v) comprises detecting a non-polymeric compound.

4. (PREVIOUSLY PRESENTED) The method of claim 2, wherein step (v) comprises detecting a non-proteinaceous compound.

5. (PREVIOUSLY PRESENTED) The method of claim 2, wherein step (v) comprises detecting a compound having a molecular weight less than 7500 amu.

6. (PREVIOUSLY PRESENTED) The method of claim 2, wherein step (v) comprises detecting a compound that is a direct product of endogenous precursors for the biosynthetic pathway.

7. (CANCELED).

8. (PREVIOUSLY PRESENTED) The method of claim 2, wherein in step (iii) the isolated genomic DNA in the clones has an average length of at least 75 kb.

9. (PREVIOUSLY PRESENTED) The method of claim 8, wherein in step (iii) the isolated genomic DNA in the clones has an average length of at least 100 kb.

10. (PREVIOUSLY PRESENTED) The method of claim 2, wherein the source of microorganisms in step (i) includes prokaryotes.

11. (PREVIOUSLY PRESENTED) The method of claim 10, wherein the source of microorganisms in step (i) includes prokaryotes of the Archaea Domain.

12. (PREVIOUSLY PRESENTED) The method of claim 11, wherein the source of microorganisms in step (i) includes Archaea cells selected from the group consisting of Crenarachaeota, Euryarachaeota, Karachaeota, and combinations thereof.

13. (PREVIOUSLY PRESENTED) The method of claim 2, wherein step (i) comprises isolating genomic DNA from a source selected from the group consisting of soil samples, insect intestines, plant rhizospheres, microbial mats, sulfur pools samples, or marine samples.

14. (PREVIOUSLY PRESENTED) The method of claim 2, wherein the source of microorganisms in step (i) includes prokaryotes having low G/C content genomes.

15. (PREVIOUSLY PRESENTED) The method of claim 2, wherein the source of uncultivated microorganisms in step (i) includes anaerobes.

16. (PREVIOUSLY PRESENTED) The method of claim 2, wherein in step (iii) the library of host cells comprises a variegated population of vectors containing different isolated genomic DNA sequences.

17. (PREVIOUSLY PRESENTED) The method of claim 16, wherein step (i) comprises isolating genomic DNA having an average length of at least 50 kilobases.

18. (PREVIOUSLY PRESENTED) The method of claim 16, wherein in step (iii) the library of host cells comprises a variegated population of vectors including isolated genomic DNA from at least 10 different microorganism species.

19. (PREVIOUSLY PRESENTED) The method of claim 2, wherein step (iii) comprises introducing the clones of step (ii) into host cells selected from the group consisting of Acetobacter, Actinomyces, Aerobacter, Agrobacterium, Azotobacter, Bacillus, Bacteroides, Bordetella, Brucella, Chlamydia, Clostridium, Corynebacterium, Erysipelothrix, Escherichia, Francisella, Fusobacterium, Haemophilus, Klebsiella, Lactobacillus, Listeria, Mycobacterium, Myxococcus, Neisseria, Nocardia, Pasteurella, Proteus, Pseudomonas, Rhizobium, Rickettsia, Salmonella, Serratia, Shigella, Spirilla, Spirillum, Staphylococcus, Streptococcus, Streptomyces, Trepanema, Vibrio, and Yersinia.

20. (PREVIOUSLY PRESENTED) The method of claim 19, wherein step (iii) comprises introducing the clones of step (ii) into host cells selected from the group consisting of Escherichia and Streptomyces.

21. (PREVIOUSLY PRESENTED) The method of claim 20, wherein step (iii) comprises introducing the clones of step (ii) into an *Escherichia coli* host cell.

22. (PREVIOUSLY PRESENTED) The method of claim 2, wherein step (ii) comprises inserting the isolated genomic DNA into a low-copy number vector.

23. (PREVIOUSLY PRESENTED) The method of claim 22, wherein step (ii) comprises inserting the isolated genomic DNA into a single-copy number vector.

24. (CURRENTLY AMENDED) The method of claim 22, wherein **step (ii) comprises inserting the isolated genomic DNA into** ~~the vector is~~ a BAC or PAC vector.

25. (PREVIOUSLY PRESENTED) The method of claim 2, wherein step (v) comprises detecting the compound produced by the host cells as a result of expression of the open reading frame sequence of step (iv) by an ability of the host cell to induce a biological or biochemical response from a test cell.

26. (PREVIOUSLY PRESENTED) The method of claim ~~2~~ 25, wherein the biological or biochemical response induced in the test cell comprises: a phenotypic change, a change in gene transcriptional rates, a change in phosphorylation states, a change in 2nd messenger formation, cell quiescence, or cell death.

27. (PREVIOUSLY PRESENTED) The method of claim 2, wherein step (v) comprises detecting the compound produced by the host cells as a result of expression of the open reading frame sequence of step (iv) by spectrometric detection.

28. (PREVIOUSLY PRESENTED) The method of claim 2, wherein step (v) comprises detecting the compound produced by the host cells as a result of expression of the open reading frame sequence of step (iv) by chromatographic detection.

29. (PREVIOUSLY PRESENTED) The method of claim 2, wherein step (v) comprises detecting the compound produced by the host cells as a result of expression of the open reading frame sequence of step (iv) using a cell-free assay.

30. (PREVIOUSLY PRESENTED) The method of claim 2, wherein step (v) comprises detecting the compound produced by the host cells as a result of expression of the open reading frame sequence of step (iv) by inducing a biological or biochemical response from the host cell.

Claims 31-40. (CANCELED).

41. (CURRENTLY AMENDED) A method for detecting a product of a biosynthetic pathway, comprising:

i) directly cloning into a replicable vector genomic DNA isolated from a complex microbial sample without an intervening step of ~~isolating or~~ culturing cells from the sample, and size-fractionated prior to any enzymatic manipulation of the DNA to facilitate its insertion into the replicable vector, wherein at least some of the genomic DNA cloned into the vector is at least 50 kb long; and then

ii) transforming the replicable vector of step (i) into host cells to obtain a library of host cells; and then

iii) expressing open reading frame sequence(s) of the genomic DNA contained in the library of host cells of step (ii); and then

iv) detecting a compound which is the product of a biosynthetic pathway that is dependent on expression of at least one of the opening reading frames of step (iii).

Claims 42-45. (CANCELED).

46. (PREVIOUSLY PRESENTED) The method of claim 2, wherein step (i) comprises lysing the microorganisms and isolating the genomic DNA from the source by further treating the source with a protease and a detergent to yield a mixture, centrifuging the mixture to yield a supernatant, extracting the supernatant with chloroform in the absence of phenol to yield a chloroform fraction containing the genomic DNA, and precipitating the DNA by adding isopropanol to the chloroform fraction.

47. (PREVIOUSLY PRESENTED) The method of claim 46, wherein step (i) further comprises size-fractionating the isolated genomic DNA prior to enzymatic manipulation of the DNA for insertion into the replicable vector of step (ii).

48. (PREVIOUSLY PRESENTED) The method of claim 47, wherein step (i) comprises size-fractionating the isolated genomic DNA via electrophoresis.